

**WE CLAIM:**

1                   1.     An isolated presenilin associated membrane protein (PAMP), or a functional  
2     fragment thereof.

1                   2.     The PAMP of claim 1, which is human PAMP (SEQ ID NO: 14).

1                   3.     The PAMP of claim 1, which is mouse PAMP (SEQ ID NO: 16) *D.*  
2     *Melanogaster* (SEQ ID NO: 18), or *C. elegans* PAMP (SEQ ID NO: 12).

4.     The PAMP of claim 1, which is a mutant PAMP.

5.     The mutant PAMP of claim 4 wherein the mutation results in biochemical  
changes similar to those induced by mutations in presenilin-1, presenilin-2, or  $\beta$ -amyloid precursor  
protein associated with familial Alzheimer's Disease.

6.     The mutant PAMP of claim 5, wherein the mutation is to an amino acid residue  
selected from the group selected from the group consisting of D336, Y337, C230, and both D336  
and Y337.

1                   7.     An isolated nucleic acid encoding the PAMP of claim 1

1                   8.     The nucleic acid of claim 7, which is human (SEQ ID NO: 13).

1                   9.     The nucleic acid of claim 7, which is mouse (SEQ ID NO: 15) *D.*  
2     *Melanogaster* (SEQ ID NO: 17), or *C. elegans* (SEQ ID NO: 11).

1                   10.    A vector comprising the nucleic acid of claim 7 operatively associated with an  
2     expression control sequence.

11. A cell transfected with the vector of claim 10.

12. A method for producing PAMP, which method comprises culturing the cell of claim 11 under conditions that permit expression of PAMP.

13. An isolated nucleic acid encoding the mutant PAMP of claim 4.

14. The nucleic acid of claim 13, wherein the mutation results in a change to an amino acid residue selected from the group consisting of D336, Y337, C230, and both D336 and Y337.

15. A vector comprising the nucleic acid of claim 13 operatively associated with an expression control sequence.

16. A cell transfected with the vector of claim 15.

17. A method for producing mutant PAMP, which method comprises culturing the cell of claim 16 under conditions that permit expression of the mutant PAMP.

18. A transgenic animal, comprising a transgene encoding presenilin associated membrane protein (PAMP) which is expressed in neural cells such that the animal detectably expresses *PAMP* mRNA.

19. The transgenic animal of claim 18, which detectably expresses PAMP protein.

20. The transgenic animal of claim 19, which processes  $\beta$ -amyloid precursor protein to produce amyloid- $\beta$  peptide.

1 21. The transgenic animal of claim 18, which is a mouse.

1 22. The transgenic animal of claim 18, wherein PAMP is human PAMP (SEQ ID  
2 NO: 14).

1 23. The transgenic animal of claim 18, wherein said PAMP is a mutant PAMP.

1 24. The transgenic animal of claim 18, further comprising a second transgene  
2 encoding a human presenilin-1, human presenilin-2 or human  $\beta$ -amyloid precursor protein, wherein  
3 the human presenilin-1, human presenilin-2, or human  $\beta$ -amyloid precursor protein is expressed at  
4 a level that permits its detection.

5 25. An animal containing a nucleic acid that expresses an endogenous presenilin  
6 associated membrane protein (PAMP) at a higher or lower level relative to expression level in a wild-  
7 type animal.

8 26. The animal of claim 25, prepared by homologous recombination mediated  
9 targeting of an endogenous PAMP gene.

10 27. The animal of claim 25, prepared by translocation of P-elements.

11 28. The animal of claim 25, prepared by chemical mutagenesis.

12 29. An isolated cell containing a nucleic acid that expresses a mutant presenilin  
13 associated membrane protein (PAMP).

14 30. The cell of claim 25, wherein the mutation results in biochemical changes  
15 similar to those induced by mutations in presenilin-1, presenilin-2 or  $\beta$ -amyloid precursor protein  
16 associated with familial Alzheimer's Disease.

1 31. A reconstituted system for measuring presenilin associated membrane protein  
2 (PAMP) activity, comprising PAMP or a functional fragment thereof, and a PAMP substrate.

1 32. The reconstituted system of claim 31, which is a whole cell.

1 33. The reconstituted system of claim 31, wherein said whole cell contains a first  
2 nucleic acid that expresses said PAMP and a second nucleic acid that expresses said substrate.

1 34. The reconstituted system of claim 31, wherein said substrate is selected from  
2 the group consisting of presenilin-1 protein, presenilin-2 protein and  $\beta$ -amyloid precursor protein.

35. A complex between a presenilin associated membrane protein (PAMP) and an  
agent which provides a detectable conformational change in said PAMP upon interaction with a  
substance being analyzed for activity against a neurodegenerative disease.

36. The complex of claim 35, further comprising presenilin 1 protein, presenilin  
2 protein,  $\beta$ -amyloid precursor protein, or a combination thereof.

1 37. A method for detecting a mutation in presenilin associated membrane protein  
2 (PAMP) associated with disease or a related neurological disorder, which method comprises detecting  
3 a variation in a sequence of a gene encoding PAMP obtained from an individual diagnosed with or  
4 suspected of having a neurodegenerative disorder.

1 38. A method for diagnosing individuals predisposed to or having a  
2 neurodegenerative disorder, which method comprises detecting a mutation in a gene encoding PAMP  
3 obtained from an individual.

1 39. The method according to claim 38, wherein detection of the mutation  
2 comprises measuring a level of transcriptional activity of the gene.

1 40. The method according to claim 38, wherein detection of the mutation  
2 comprises measuring PAMP activity.

1 41. The method of claim 40, wherein said PAMP activity comprises PAMP  
2 expression level or activity of a product of a PAMP modified substrate.

1 42. A method for identifying a compound that modulates PAMP activity, which  
2 method comprises detecting modulation of PAMP expression in a transgenic animal that expresses  
3 PAMP, wherein the animal is contacted with the compound.

4 43. A method for identifying a compound that modulates PAMP activity, which  
5 method comprises detecting a change in PAMP activity in the reconstituted system of claim 31  
6 contacted with a test compound.

7 44. A method for identifying a compound that modulates PAMP activity, which  
8 method comprises detecting a conformational or functional change in PAMP in the complex of claim  
9 35 contacted with a test compound.

1 45. The method of claim 44, wherein the compound is a protein that interacts with  
2 PAMP.

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